PATENT
Docket No. 524022000100

CERTIFICATE OF MAILING BY "FIRST CLASS MAIL"

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

6-27-02 RHEA AMIO Rhea Amio

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Dexu ZHU, et al

Serial No.: 09/975,136

Filing Date: October 10, 2001

For: METHODS AND COMPOSITIONS FOR TREATING OR PREVENTING BACTERIAL INFECTION

Examiner: Paul A. Zucker

Group Art Unit: 1623

DECLARATION OF MING-WEI WANG PURSUANT TO 37 C.F.R. §1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

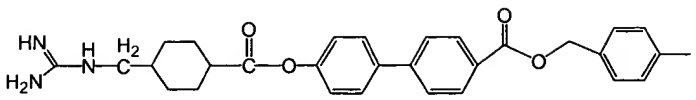
Dear Sir:

I, Ming-Wei Wang, declare as follows:

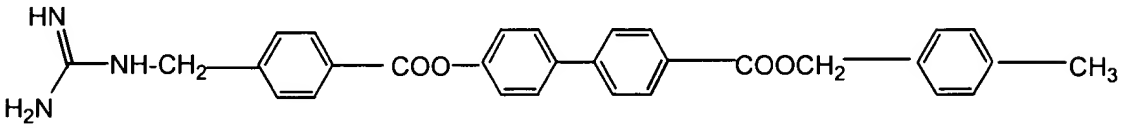
1. I am one of the co-inventors of the subject matter claimed in the above-referenced application.

2. I have studied the Kamoda patent cited in the March 27, 2002 Office Action and found that the compound disclosed therein:

EXHIBIT B



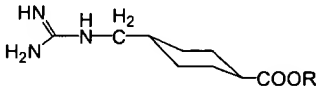
is structurally and stereochemically different from one of the compounds (NE-2001)



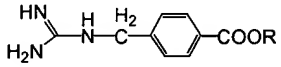
claimed in the present application.

3. The compound disclosed in Kamoda has a cyclohexane ring in between the carboxyl group and the methyl group whereas NE-2001 has an aromatic ring at the corresponding position. Therefore, the two compounds are structurally different.

4. The core structure of the compound disclosed in Kamoda is trans-guanidinomethyl cyclohexyl, which stereochemically has a chair form as follows:



In contrast, NE-2001 of the present application stereochemically has a plane form as follows:



5. My colleagues and I have conducted experiments demonstrating advantage of NE-2001 over the compound disclosed in Kamoda. First, the IC_{50} of NE-2001 for inhibiting one of its targets, Proteinase In, is 1.00 μM (See Figure 1 attached herein). The IC_{50} of the compound disclosed in Kamoda (shown as TG44 in Figure 1) for inhibiting Proteinase In is 1.54

μM. Therefore, NE-2001 is a more potent inhibitor. In addition, NE-2001's solubility in methanol is almost twice of that of the compound disclosed in Kamoda (shown as TG44 in Table 1). NE-2001 has a solubility of 333 millilitres methanol per gram of NE-2001. The compound disclosed in Kamoda (shown as TG44 in Table 1) has a solubility of 540 millilitres methanol per gram of TG44. NE-2001's higher solubility in methanol is beneficial for its formulation and for penetrating the cell wall of *H. pylori* cells.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to by true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

Executed at San Diego, California, on June 14, 2002.

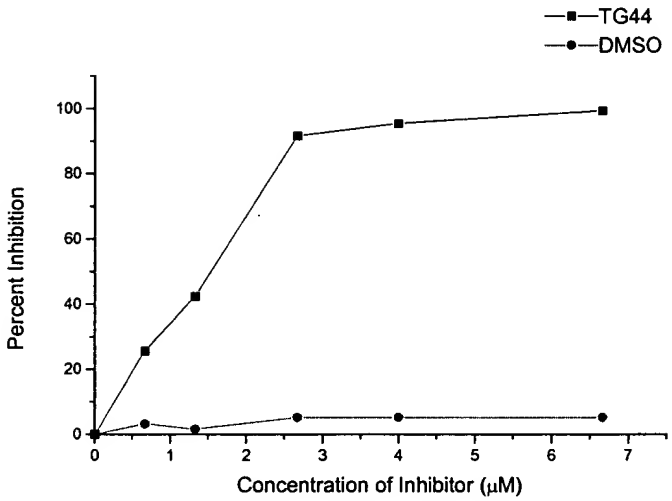
Ming-Wei Wang

Figure 1. Inhibitory Effects of TG44* and NE-2001 on the Proteinase In from *E. coli*

Inhibitor TG44:

	F.S.	% Inh.	
Standard 1:	43.4		
Standard 2:	44.5	mean 43.9	0
0.67uM	32.6		25.7
1.3	25.3		42.4
2.7	3.7		91.6
4.0	2.0		95.4
6.7	0.3		99.3

IC_{50}=1.54μM

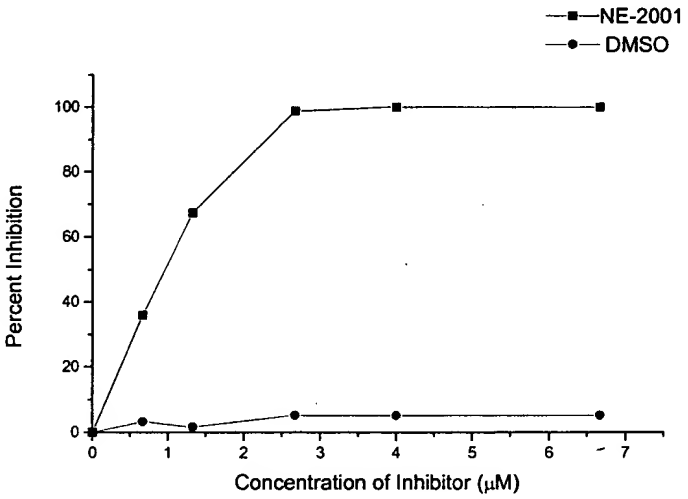


* TG44: 4-Methybenzyl 4'-[trans-4(guanidinomethyl) cyclohexylcarbonyloxy] biphenyl - 4 carboxylate monohydrochloride

Inhibitor NE-2001:

	F.S.	% Inh.	
Standard 1:	43.4		
Standard 2:	44.5	mean 43.9	0
0.67uM	28.1		36.0
1.3	14.3		67.4
2.7	0.51		98.8
4.0	0		100
6.7	0		100

IC_{50}=1.00μM



sd-98688

EXHIBIT B

Table 1. Solubility Testing Results

1. Experimental objective: solubility study
2. Experimental method: according to the Chinese Pharmacopoeia (2000 Edition), Volume 2, Appendix
3. Sample name: NE-2001 (Batch #: 011218) and TG44
4. Experimental results: see the table below
5. Reporting date: 4/27/2002

Sample name	Solvent	Sample weight (mg)	Solvent volume (ml)	Solution concentration (g/ml)	Result	Solubility
NE-2001 (Bat. #: 011218)	Methanol	10.52	3.50	1/333	Soluble	Slightly soluble
	Water	1.20	13	/	Not completely soluble	Almost insoluble
	Ethyl acetate	1.00	11	/	Not completely soluble	Almost insoluble
	Chloroform	1.38	14	/	Not completely soluble	Almost insoluble
	Ether	1.31	14		Not completely soluble	Almost insoluble
	0.1 mol/L Hydrochloride	1.23	13	/	Not completely soluble	Almost insoluble
	0.1 mol/L Sodium hydroxide	1.24	13	/	Not completely soluble	Almost insoluble
TG44	Methanol	11.12	6.00	1/540	Soluble	Slightly soluble
	Water	0.96	10	/	Not completely soluble	Almost insoluble
	Ethyl acetate	1.14	12	/	Not completely soluble	Almost insoluble
	Chloroform	1.05	11	/	Not completely soluble	Almost insoluble
	Ether	0.87	10	/	Not completely soluble	Almost insoluble
	0.1 mol/L Hydrochloride	1.15	12	/	Not completely soluble	Almost insoluble
	0.1 mol/L Sodium hydroxide	0.96	10	/	Not completely soluble	Almost insoluble

EXHIBIT B